REMARKS

The invention relates in part to assay devices that utilize mass transport by laminar flow of a sample through the layers of the device. Because laminar flow overcomes limitations in sensitivity caused by diffusion boundary formation as an analyte binds to a surface, the devices of the present invention can provide advantageous capture efficiencies.

Claims 1-50 are pending in the instant application, and claims 1-12, 18-34, and 36-50 under consideration by the Examiner. Claim 9 is amended herein. The amended claim is fully supported by the specification, and does not introduce new matter or require a new search. The amendment simply clarifies the claimed invention using preferred terminology, and is not intended to further limit the claim, and should not be taken to do so.

Notwithstanding the foregoing, Applicants expressly reserve the right to pursue subject matter no longer claimed in the instant application in one or more applications which may claim priority hereto. Applicants respectfully request reconsideration of the claimed invention in view of the foregoing amendments and the following remarks.

Drawings:

Applicants gratefully acknowledge the Examiner's comments concerning the informal drawings filed in the instant application. Appropriate formal drawings are submitted together with this submission.

Non Art-Related Remarks

35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claim 9 under 35 U.S.C. § 112, second paragraph, contending that the claim is allegedly indefinite in reciting the phrase "absorbent material.". Applicants respectfully traverse the rejection.

When determining definiteness, the proper standard to be applied is "whether one skilled in the art would understand the bounds of the claim when read in the light of the specification." *Credle v. Bond*, 30 USPQ2d 1911, 1919 (Fed. Cir. 1994). See also *Miles Laboratories, Inc. v.*

Shandon, Inc., 27 USPQ2d 1123, 1127 (Fed. Cir. 1993) ("If the claims read in the light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more.") (emphasis added).

The Examiner contends that it is allegedly unclear whether the "absorbent material" in claim 9 is meant to refer to "light absorbent" or "liquid absorbent." Paper No. 18, paragraph bridging pages 2-3. Applicants respectfully submit that the phrase absorbent material is clearly defined in the instant specification, *e.g.*, on page 14, lines 25-27. Because one skilled in the art would understand that such absorbent material refers to a liquid absorbent material, the instant claims fully comply with the definiteness requirement of 35 U.S.C. § 112, second paragraph.

Nevertheless, in an effort to advance prosecution, Applicants have amended claim 9 to recite "a liquid absorbent material," thus rendering the rejection moot. Applicants note that the amendment does not further limit the claims, but rather inserts a definition of a claim term from the specification into the claims. Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. § 112, second paragraph.

Art-Related Remarks

35 U.S.C. § 102

The Examiner has rejected claims 18, 19, and 23 under 35 U.S.C. § 102(b) as allegedly being anticipated by Brecht *et al.*, Anal. Chim. Acta 311: 289-299 (1999). Applicants respectfully traverse this rejection.

In order to anticipate a claim, a single prior art publication must provide each and every element set forth in the claim. Furthermore, the claims must be interpreted in light of the teachings of the specification. *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). *See* also MPEP §2131.

As discussed in Applicants' previous response, the optical assay devices of instant claims 18, 19 and 23 comprise a support and an optically functional layer configured and arranged to provide laminar flow through or through and across the layers of the device. Thus, at a minimum, the optical assay device must allow laminar flow through the layers of the device. In

contrast, as noted in Applicants previous responses, the Brecht *et al.* publication does not provide any devices in which laminar flow is provided. Moreover, even if the Examiner is correct that laminar flow is provided by the devices disclosed in the Brecht *et al.* publication, reagent flow in such devices does not occur through the layers of the device, but rather across the device surface.

In this regard, Applicants respectfully direct the Examiner's attention to the detailed arguments previously made in the previous response submitted on December 15, 2000, pages 3-6. In particular, Applicants provided evidence that laminar flow need not be parallel to a flat surface, as contended by the Examiner in Paper No. 15, pages 3-4. Thus, the skilled artisan would reasonably understand that flow in the instantly claimed devices may occur through the various layers, and yet still be laminar flow. This feature of the instantly claimed device is not disclosed by Brecht *et al.* publication.

Therefore, because Brecht *et al.* publication does not teach each and every element set forth in the claims, no *prima facie* case of anticipation has been established. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

35 U.S.C. §103

The Examiner has maintained the rejection of claims 1, 2, 7, 9, 18-26 and 36 under 35 U.S.C. §103(a), as allegedly being unpatentable over Oberhardt, U.S. Patent No. 4,849,340 ("the '340 patent"). Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness, three criteria must be met: there must be some motivation or suggestion, either in the cited publications or in knowledge available to the ordinarily skilled artisan, to modify or combine the publications; there must be a reasonable expectation of success in combining the publications; and the publications must teach or suggest all of the claim limitations. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991) See also MPEP §2143.

The Examiner contends that the devices disclosed in the '340 patent allegedly comprise an "optically active layer," as that term is used in the instant claims. Applicants respectfully submit that the Examiner has misinterpreted the cited patent in this regard. As described in the

instant specification, an "optically active layer" is a layer in a device that is configured to produce a signal due solely to the change in optical thickness or mass bound to the surface of the device. This signal is generated due to changes in the optical characteristics of the optically active layer, and not due to the optical properties (*e.g.*, light scattering, the presence of a fluorescent label, *etc.*) of the sample material. *See, e.g.*, specification, page 5, lines 1-7; page 15, line 26, through page 16, line 2; and page 20, lines 6-27. No devices comprising such an optically active layer are disclosed in the '340 patent. Instead, the devices disclosed in the '340 patent generate signals using only methods that rely on light scattering or detectable labels.

The Examiner points to devices using "optical methods of measurement" disclosed in the '340 patent as allegedly being equivalent to the devices of the instant claims. For example, the Examiner states that "a wide variety of light paths for detection is described including waveguide practice." Paper No. 18, page 4. Applicants respectfully submit that whether or not the '340 patent describes the use of a waveguide is irrelevant to the instant claims, as waveguides are merely "light pipes" that are used to propagate optical energy from one point to another. Moreover, while the Examiner argues that such waveguides allegedly "[define] an antireflective layer," antireflective layers are not an inherent characteristic of waveguides. If the Examiner believes that antireflective layers are, in fact, inherent in these devices, Applicants respectfully request that the Examiner provide evidence, based on sound scientific principles, as to why the skilled artisan would consider such to be the case. *See*, MPEP §§ 2144.01-2144.02.

The Examiner also contends that the '340 patent refers to "light measurement via reflection practice or absorption." Paper No. 18, page 4. Applicants respectfully submit that, while the '340 patent may refer to such methods for generating a signal, none of these methods disclose or suggest the use of an "optically active layer" as a source of a detectable signal. For example, in column 19, line 44, through column 20, line 52, the '340 patent discloses a reflectance method. Changes in the reflectance signal in this method are generated, not by a device surface, but rather from particles in solution. *See,* '340 patent, column 19, lines 53-56 ("There is also provided a light source for providing incident light and a detector positioned for detecting light rays reflected from the sample within the reaction volume") (emphasis added).

Similarly, the '340 patent discloses another reflectance method in column 21, lines 46-65, which relies on the Kubelka-Monk theory, a theory that relates to the light scattering properties of turbid media, for generating a signal. *See, e.g.*, '340 patent, column 21, lines 64-65. As in the first reflectance method discussed above, particles in solution, and not changes in optical thickness or mass on an optically active surface, are responsible for generating a change in reflectance within the device. For the Examiner's convenience, Applicants submit herewith as Appendix B several web publications related to Kubelka-Monk theory.

The Examiner points with particularity to column 11, lines 6-17 of the '340 patent, contending that "optically active reflecting layers are described." Paper No. 18, page 4. But, consistent with the discussion provided above, this section indicates that the devices disclosed in the '340 patent are "useful in making measurements based on the transmission or absorbance of light by the fluid within the reaction volume. '340 patent, column 11, lines 9-11, emphasis added. Nothing in this section, or indeed in the entire '340 patent, discloses or suggests any devices comprising an optically active layer, as the term is used in the instant claims.

At best, then, the '340 patent discloses the use of a simple reflective surface within the device, to provide internal reflectance in a waveguide (*see, e.g.*, column 11, line 6-8) or as a means to detect light that has not been scattered by particles in a solution (*see, e.g.*, column 21, lines 46-65). Even if the Examiner is correct that this may be considered an optically active layer (which, as discussed above, is not a correct interpretation), the Examiner correctly recognizes that the '340 patent does not disclose laminar flow through this reflective surface. But the Examiner contends that "it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to optionally construct and utilize a device with laminar flow through various layer selections. Paper No. 18, page 5. The only alleged motivation the Examiner suggests for doing so is that the '340 patent "describes a wide variety of [elements] which are selectable given the various sections directed to these practices." *Id.*

Applicants respectfully submit that this is not a motivation to modify the devices of the cited patent; instead, it is merely a statement that the Examiner believes that modification of the cited publication to provide the instantly claimed invention is possible. As such, it is not sufficient to support a *prima facie* case of obviousness. *See, e.g.*, MPEP §2143.01 (The fact that

references may be combined or modified does not render the combination or modification obvious unless the prior art suggests the desirability of the combination or modification; the fact that the claimed invention is within the capabilities of one skilled in the art, without some objective reason to provide the claimed invention, cannot support a *prima facie* case of obviousness). Nothing in the Examiner's alleged *prima facie* case suggests the desirability of providing any device in which laminar flow occurs through the reflective layer of the devices disclosed in the '340 patent.

Therefore, because the cited patent fails to teach or suggest all of the limitations set forth in the instant claims, and because nothing in the Examiner's alleged *prima facie* case provides any motivation to modify the devices of the cited patent to provide the instantly claimed invention, Applicants respectfully request that the rejection under 35 U.S.C. §103 be reconsidered and withdrawn.

35 U.S.C. 101

The Examiner has provisionally rejected claims 1-12, 18-34 and 36-50 under 35 U.S.C. 101 as allegedly claiming the same invention as that of claims 1-12, 18-34 and 36-50 of co-pending application serial no. 09/675,518; and under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-12, 18-34 and 36-38 of application serial no. 09/675,518. Applicants respectfully traverse these rejections.

The Examiner's attention is directed to the Preliminary Amendment filed on September 28, 2000 for the co-pending application at issue, in which Applicants requested the cancellation of all originally filed claims, and entered new claims 51-91 that are unrelated to the instant claims. For the Examiner's convenience, a copy of the Preliminary Amendment is attached herewith as Appendix C. In light of the status of the claims in application serial no. 09/675,518, Applicants respectfully request that the Examiner withdraw the double patenting rejections rejection.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully submit that the pending claims are in condition for allowance. An early notice to that effect is earnestly solicited. Should any matters remain outstanding, the Examiner is encouraged to contact the undersigned at the address and telephone number listed below so that they may be resolved without the need for additional action and response thereto.

Respectfully submitted,
FOLEY & LARDNER

Dated: January 2, 2002

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Appendix A: Marked-up claim, indicating amendments.

9. (Amended) The device of any of claims 1, 2, 3, 4, 5 or 6, wherein said device further comprises [an] a liquid absorbent material surrounding said optically functional layer or beneath said support.

Colour Science Glossary

Kubelka-Munk Theory

A theory devised by Kubelka and Munk describing the optical property of a turbid medium which absorbs and scatters light.

Compiled by Ronnier Luo and Peter Rhodes.

Light and MatterLight and Matter

What is the color spectrum?

The modern understanding of color originated in the discovery of the spectral nature of light by Isaac Newton in the 1600s. Newton's famous experiments demonstrated that light consists of energy of different wavelengths. We now know that the eye is sensitive to a broad band of wavelengths in the approximate range 350-750 nm. The visible spectrum represents only a small fraction of the full electromagnetic spectrum. Within the visible spectrum certain wavelengths give rise to certain visual sensations. For example, the shorter wavelengths are perceived to be violet and blue.

BACK

What happens when light strikes the surface of a material?

When light strikes a surface there are two things that can happen:
(i) the change in refractive index can cause light to be reflected by the surface and this surface-reflected light is called specular reflection;
(ii) light that is not reflected at the surface can penetrate the body of the material although as it passes through the surface the change in refractive index will cause the light to be refracted.
Light may pass completely through a material, in which case we say that it has been transmitted. Alternatively the light may be absorbed by the material or it may be scattered. Light that is scattered or reflected may eventually pass out of the front, back, or side of the material.

BACK

How is light absorbed?

Light can be absorbed by materials according to a number of mechanisms that include atomic vibrations and rotations, ligand-field effects, molecular orbitals, and charge transfer. It is very often the case that specific quantities of light (energy) are absorbed by a specific material and thus the light absorbtion properties of materials are usually wavelength selective.
The energy that is absorbed by molecules can be dissipated as kinetic and heat energy, but sometimes the energy can be re-emitted. Fluourescence and phosphorescence are phenomena that result from the re-emission of absorbed light energy: in both cases the re-emitted energy is at a longer wavelength than the light originally absorbed.

BACK

Appendix C

09/675,518

Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Drewes et al.

Serial No.: Not Yet Assigned

Filed: Herewith

For: METHODS AND DEVICES FOR MASS TRANSPORT ASSISTED OPTICAL ASSAYS

Group Art Unit: Not Yet Assigned

Examiner: Not Yet Assigned

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

In conjunction with the divisional patent application filed herewith, please enter the following amendments and consider the following remarks.

IN THE CLAIMS

Please cancel all of the currently pending claims, and enter the following new claims:

CERTIFICATE OF MAILING
(37 C.F.R. §1.10)

I hereby certify that this paper (along with any referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as 'Express Mail Post Office To Addressee' in an envelope addressed to the Commissioner for Patents, Washington, D.C. 20231.

EL676079979 US
Express Mail Label No.

September 28, 2000
Date of Deposit

Gretchen Dieckmann
Name of Person Mailing Paper

Gretchen Dieckmann
Signature of Person Mailing Paper

Claim 51. A support comprising a surface on which an assay for an analyte of interest can be performed, comprising:

an attachment layer comprising diamond-like carbon on the support surface, wherein the attachment layer captures the analyte of interest for detection in the assay by binding the analyte directly to the diamond-like carbon.

Claim 52. A support according to claim 51, wherein the attachment layer comprises a layer of diamond-like carbon of between about 50 Å to about 3000 Å in thickness.

Claim 53. A support according to claim 51, wherein the degree of hydrophobicity of the attachment layer is determined by varying the sp^2 and sp^3 character of the diamond-like carbon.

Claim 54. A support according to claim 51, wherein the diamond-like carbon is configured to function as an antireflective layer.

Claim 55. A support according to claim 51, wherein the support further comprises an optically functional layer interposed between the support surface and the attachment layer.

Claim 56. A support according to claim 51, wherein the support provides a change in optical thickness upon binding of the analyte capable of attenuating one or more wavelengths of light.

Claim 57. A support according to claim 51, wherein the support is configured to provide laminar flow through or across the support.

Claim 58. A support according to claim 51, wherein the attachment layer comprises diamond-like carbon in a form selected from the group consisting of synthetic diamond, natural diamond, industrial diamond, monocrystalline diamond, resin-type diamond, polycrystalline diamond, amorphous carbon with diamond-like hardness and surface energy properties, amorphous hydrogenated diamond-like carbon, and non-crystalline to crystalline carbon films with diamond-like hardness and surface energy properties.

Claim 59. A support according to claim 51, wherein the diamond-like carbon comprises non-carbon material.

Claim 60. A support according to claim 59, wherein the non-carbon material is selected from the group consisting of hydrogen, silicon, and nitrogen.

Claim 61. A support according to claim 51, wherein the support comprises a material that is not compatible with high temperatures.

Claim 62. A support according to claim 61, wherein said high temperature is greater than 100°C.

Claim 63. A support according to claim 61, wherein the material that is not compatible with high temperatures is selected from the group consisting of cellulose acetate, PETE, polyester, polycarbonate, nylon, filter paper, polysulfones, polypropylene, and polyurethane.

Claim 64. A support according to claim 61, wherein the diamond like carbon has a hardness of about 15 to about 50 Gpa.

Claim 65. A support according to claim 61, wherein the attachment layer has a refractive index of about 1.5 to about 2.2.

Claim 66. A support according to claim 51, wherein said support is a biosensor.

Claim 67. A support comprising a surface on which an assay for an analyte of interest can be performed, comprising:

an attachment layer comprising a layer of diamond-like carbon of between about 50 Å to about 500 Å in thickness on the support surface, wherein said attachment layer specifically captures said analyte by binding said analyte to a capture molecule bound to the diamond-like carbon.

Claim 68. A support according to claim 67, wherein said capture molecule is selected from the group consisting of an antigen, an antibody, a receptor, a nucleic acid, an RNA,

a DNA, a polysaccharide, a lipopolysaccharide, an enzyme, a protein, a microorganism, a hapten, a drug, a ligand, and a chelator.

Claim 69. A support according to claim 67, wherein the degree of hydrophobicity of the attachment layer is determined by varying the sp^2 and sp^3 character of the diamond-like carbon.

Claim 70. A support according to claim 67, wherein said diamond-like carbon is configured to function as an antireflective layer.

Claim 71. A support according to claim 67, wherein said support further comprises an optically functional layer interposed between said surface and said attachment layer.

Claim 72. A support according to claim 67, wherein said support provides a change in optical thickness upon binding of said analyte capable of attenuating one or more wavelengths of light.

Claim 73. A support according to claim 67, wherein said support is configured to provide laminar flow through or across said support.

Claim 74. A support according to claim 67, wherein said attachment layer comprises diamond-like carbon in a form selected from the group consisting of synthetic diamond, natural diamond, industrial diamond, monocrystalline diamond, resin-type diamond, polycrystalline diamond, amorphous carbon with diamond-like hardness and surface energy properties, amorphous hydrogenated diamond-like carbon, and non-crystalline to crystalline carbon films with diamond-like hardness and surface energy properties.

Claim 75. A support according to claim 67, wherein the diamond-like carbon comprises non-carbon material.

Claim 76. A support according to claim 75, wherein the non-carbon material is selected from the group consisting of hydrogen, silicon, and nitrogen.

Claim 77. A support according to claim 67, wherein the support comprises a material that is not compatible with high temperatures.

Claim 78. A support according to claim 77, wherein said high temperature is greater than 100°C.

Claim 79. A support according to claim 77, wherein the material that is not compatible with high temperatures is selected from the group consisting of cellulose acetate, PETE, polyester, polycarbonate, nylon, filter paper, polysulfones, polypropylene, and polyurethane.

Claim 80. A support according to claim 77, wherein the diamond like carbon has a hardness of about 15 to about 50 Gpa.

Claim 81. A support according to claim 77, wherein the attachment layer has a refractive index of about 1.5 to about 2.2.

Claim 82. A support according to claim 67, wherein said support is a biosensor.

Claim 83. A method of assaying for the presence or amount of an analyte of interest in a sample, comprising:

contacting a support according to claim 51 with the sample, whereby analyte in the sample binds directly to the diamond like carbon;

contacting the bound analyte with a reagent that specifically binds to the bound analyte; and

detecting the bound analyte by measuring a mass change on the support surface.

Claim 84. A method according to claim 83, wherein mass change is detected by measuring an optical property of the support.

Claim 85. A method according to claim 84, wherein the optical property is selected from the group consisting of a change in reflectivity, a change in transmittance, a change in absorbance, extinction of a specific wavelength of light, enhancement of a specific wavelength of light, and a change in polarization of incident light.

Claim 86. A method according to claim 84, wherein the reagent that specifically binds to the bound analyte comprises a signal generating element or a mass enhancing element.

Claim 87. A method of assaying for the presence or amount of an analyte of interest in a sample, comprising:

contacting a support according to claim 67 with the sample, whereby analyte in the sample binds to the capture molecule bound to the diamond like carbon; and

detecting the bound analyte by measuring a mass change on the support surface.

Claim 88. A method according to claim 87, wherein mass change is detected by measuring an optical property of the support.

Claim 89. A method according to claim 88, wherein the optical property is selected from the group consisting of a change in reflectivity, a change in transmittance, a change in absorbance, extinction of a specific wavelength of light, enhancement of a specific wavelength of light, and a change in polarization of incident light.

Claim 90. A method according to claim 87, wherein the assay further comprises contacting the bound analyte with a reagent that specifically binds to the bound analyte.

Claim 91. A method according to claim 90, wherein the reagent that specifically binds to the bound analyte comprises a signal generating element or a mass enhancing element.

REMARKS

SUMMARY

The instant invention relates in part to supports on which an assay for one or more analytes can be performed. In particular, the invention discloses supports that are configured to capture analytes on a surface for detection, preferably using optical methods. In certain embodiments, a layer of diamond-like carbon can be used to directly or indirectly bind an antigen of interest.

Applicants have cancelled all of the claims filed with the application, and enter new claims 51-91. The new claims are fully supported by the specification as filed. For example, the specification describes a support comprising a diamond-like carbon attachment layer on page 18, lines 26-29, and page 42, lines 17-29; specific and non-specific binding on an attachment layer on page 11, lines 7-20; various capture molecules on page 35, lines 21-26, and originally filed claim 43; selecting diamond-like carbon having a specific degree of hydrophobicity on page 40, lines 6-20; configuring diamond-like carbon to function as an antireflective layer on page 43, lines 3-19; interposing an optically functional layer between a surface and an attachment layer on page 19, lines 1-6; a support providing a change in optical thickness upon analyte binding on page 20, lines 10-27; a support configured to provide laminar flow on page 27, lines 10-20; various forms of diamond-like carbon on page 19, line 26, through page 20, line 5; a support configured as a biosensor on page 42, line 27, through page 43, line 2; and diamond-like carbon comprising non-carbon materials on page 38, line 18, through page 39, line 2.

CONCLUSION

Applicants respectfully submit that the pending claims are in condition for allowance. An early notice to that effect is earnestly solicited. Should any matters remain outstanding, the Examiner is encouraged to contact the undersigned at the address and telephone number listed below so that they may be resolved without the need for additional action and response thereto.

Respectfully submitted,
Brobeck, Phleger & Harrison LLP

Dated: 9/28/00

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